REMARKS

Claims 1, 8, 14, 18, 31 and 38 are pending. Claims 1, 8, 14, 18 and 31 have been amended. Claim 38 has been cancelled. Claim 40 has been added.

Because of the amendments do not introduce any new matter, Applicant respectfully requests that the amendments be entered.

Rejections Under 35 USC §103

The examiner asserts that Claims 1, 8, 14, 18, 31 and 38 are rejected under 35 USC §103 for the reasons previously set forth on paper No. 28, Section 5, pages 2-6 and the previous rejections cited in paper No.28, Section 5, pages 2-6. Claim 38 has been cancelled.

From paper No.28, Section 5, pages 2-6 and paper No.31, pages 2-12.

Hadvary et. al. US Patent # 4,598,089 recites oral administration of Xenical (Orlistat). Xenical is a lipase inhibitor resulting from the byproduct of the cultivation of Streptomyces toxytricini. Xenical is an N-formylleucine derivative used for the treatment and/or prevention of obesity. This product is not related to an anti-lipase antibody structurally or functionally. Although no mode of action is suggested for Xenical, it is assumed that it binds to the active binding site of lipase. The present invention since it is a polyclonal antibody it can bind to several areas of lipase not just the active site. An enzyme need to maintain its tertiary structure in order to function and anything that alters that structure can inhibit the enzyme activity, this is the case of the anti-lipase polyclonal antibody which bind to several places on the tertiary structure of lipase. Four more patents have been published recently suggesting the use of lipase inhibitors for the treatment of obesity. Mandeville, et. al. US # 6,267,952 , disclose a polymer that inhibit lipase, the polymer binds to the active site of the enzyme making it inactive. Chapus US # 6,432,400 disclose a treatment of obesity with a lipase inhibitor consisting of a c-terminal fragment of pancreatic lipase (see claim 6 in particular, claiming inhibition of lipase and therefore inhibiting lipolysis of the substrate). Isler et. al. US # 5,540,917 suggest the use of combination of a lipase inhibitor and thickener (fiber) to treat obesity. Hug et. al. US # 6,358,522 suggests a pharmaceutical compositions containing lipase inhibitors. These patents have the same function as compound suggested by Hadvary et al US Patent # 4,598,089 but they are of different source and structurally different.

Moloney (Livestock Prod, Sci. 1995, 42:239-245) and Flint (Proc. Nutrition Soc. 1992, 51:433-439) suggest the use of immunity to decrease adiposity in animals. This immune response by neutralizing, inhibiting or mimicking gastro-intestinal compounds and/or adipose cell components, may decrease adiposity in the animal by affecting direct lipogenesis in the adipose tissue. The present invention does not suggest any effect on the adipose tissue, what is suggested is the decrease in fat absorption limited to the gastro-intestinal tract of the animal. In order for this invention to have an affect on the adipose tissue; first, the antigen and second, the mode of administration (orally fed) are not the adequate because the antibody in order to be absorbed through the gastro-intestinal wall has to be partitioned into peptides or amino acids. Second, although lipase is a GI substance its immunoneutralization (Flint, Proc. Nutrition Soc. 1992, 51:433-439) will have a detrimental effect on the adipose tissue, lipase is not a good antigen to destroy or alter adipose tissue, one good antigen as suggested by Moloney (Livestock Prod, Sci. 1995, 42:239-245) is the adipocyte cell membrane. There is lipase present in the adipocytes which is needed for the release of fatty acids to the blood stream, having anti-lipase antibodies in the adipocytes will prevent release of triglycerides and fatty acids when needed (Durplus, et. al. 2001, New Avenues of Research in Fatty Acid Oxidation and Ketone Body Metabolism pg. 13; Albright and Stern, 1998, Adipose Tissue, pg. 5). The present invention does not try to reduce the fat content of meat or improve the quality of meat by immunological methods, there are several nutritional and chemical methods that can result in a lean animal, the use of beta-adrenergics and conjugated linoleic acid are examples (US patents #5,554,646, 5,851,572 and 5,919,451). By limiting the intake of fat, as in the present invention, it will not necessarily result in a lean animal, animals can de novo synthesize fatty acids and store them in the adipocytes; animals can become fat just by consuming carbohydrates in excess of their metabolic requirement.

Ohkaru et al and JP 02150294 disclose the use of monoclonal anti-lipase antibodies for the quantification and activity of lipase in in-vitro test. They do not suggest the use of these antibodies for the inhibition of lipase in-vivo or their use on the inhibition of fat absorption in the gastro-intestinal tract of an animal. The present invention is novel because it was thought that since avian or mammalian antibodies are proteins they will be destroyed or deactivated because of the acidity of the stomach. Newborn mammals during the first 24

hours of life have a permeable intestine able to absorb intact proteins like antibodies in colostrum. We as well as other inventors have found that the antibody remains active in the gastro-intestinal tract of the growing and adult animal and those antibodies have an active role when administered orally.

Several patents have demonstrated the effectiveness of orally administered antibody. In special: Cook, et al. US Patent # 5,989,584 disclose a method of increasing food efficiency in both avian and mammals by using avian antibodies to gut peptides such as cholecystokinin to elicit a biological response which decreases gastrointestinal motility, reduces satiety or improves feed efficiency; and Cook, et al. US Patent 5,827,517 disclose a method of modulating feeding behavior in animals, comprising the step of feeding an avian antibody to a gut peptide to an animal by oral administration in order to alter a physiological effect of said peptide relating to feeding or growth behavior. Both patents use a gastro-intestinal compound that has already defined functions as satiety hormone and decreasing residence time of food in the GI tract. Inhibiting this hormone, CCK, did not affect the adipose tissue but increase feed intake and increase the residence time of nutrients in the GI tract so more nutrients are utilized rather that excreted. It is seen here that modification or inhibition of the function of a hormone by avian antibodies rather than by drugs or feed are considered different even though they produce the same response.

Stolle, et al. US Patent # 5,932,250 discloses a treatment of vascular disorders particularly arteriosclerosis and atherosclerosis in warm-blooded animals. The invention encompasses the ingestion, by warm-blooded animals, of eggs or egg fractions derived from female avian that have been hyperimmunized with specific bacterial antigens or groups of bacterial antigens. This same result can be obtained with the use of antibiotics since the purpose of this patent is to reduce the bacterial load in the intestine so less of the bile acid is converted into its secondary components, deoxycholic and lithocolic acid, which are needed for the re-synthesis of bile in the liver. By decreasing the re-absorption of bile in the intestine more cholesterol must be shuttle to the liver to satisfy bile production therefore a decrease on cholesterol in blood.

Kodama , et al. US Patent # 6,419,926 discloses antibodies obtained from eggs laid by hens which have been immunized against urease of Helicobacter pylori as an antigen, and

specific antibodies obtained from eggs laid by hens which have been immunized against flagella of Helicobacter pylori as an antigen. These antibodies are useful for the prevention or treatment of gastritis, gastric ulcers and duodenal ulcers caused by infection of Helicobacter pylori. Similar results can be obtained with antibiotics; urease antibodies and antibiotics reduce H. pylori by different means.

Other patents are shown as reference of the use of avian antibodies in different forms of administration. Williams, et al. US Patent # 6,365,158 discloses an avian antitoxin to *C. difficile toxin B* designed so as to be orally administrable in therapeutic amounts and may be in any form (i.e., as a solid or in aqueous solution). Kink , et al. US Patent # 6,290,960 discloses a method of treating Clostridium difficile intoxication with an avian antibody reactive with Clostridium difficile toxin. Williams , et al. US Patent # 6,080,400 discloses a neutralizing avian antibody directed against verotoxins. This antitoxin is designed so as to be administrable in therapeutic amounts and may be in any form (i.e., as a solid or in aqueous solution). Kink , et al. US Patent # 5,736,139 discloses a neutralizing antitoxin directed against C. difficile toxins. These antitoxins are produced in avian species using soluble recombinant C. difficile toxin proteins. The avian antitoxins are designed so as to be orally administrable in therapeutic amounts and may be in any form (i.e., as a solid or in aqueous solution). Solid forms of the antitoxin may comprise an enteric coating. Stafford , et al. US Patent # 6,346,247 discloses an avian antibody for the prevention and treatment of autoimmune disease in humans (as well as other animals). Antibodies and receptors to the proinflammatory cytokines IL-2, TNF, IL-12 and IFN-gamma are employed (along with other antibodies to such cytokines). Such antibodies administered orally are effective at delaying the onset of autoimmune disease. Sterling , et al. US Patent # 5,753,228 discloses the use of antibodies on egg yolks and egg yolk for the prevention and treatment of intestinal parasitic infections. Kink , et al. US Patent # 6,395,273 describe a treatment of inflammatory bowel disease in animals, including humans by administering avian polyclonal antibodies directed to TNF. Adalsteinsson , et al. US Patent # 6,086,878 disclose a method to increase muscle protein or reducing fat in an animal. The method comprises administering to the animal an effective amount of a composition comprising a gastrointestinal neuro-modulator avian or mammalian antibody in order to neutralize the gastrointestinal neuro-modulator. Pimentel US

Patent # 5,741,489 discloses a method for increasing feed conversion efficiency in mammals, such as swine, wherein the mammal is fed a diet containing an avian antibody produced using the enzyme urease as the antigen.

Combination Moloney (Livestock Prod, Sci. 1995, 42:239-245) and Flint (Proc. Nutrition Soc. 1992, 51:433-439) the present invention do not suggest an effect on the adipose tissue or an improvement on the quality of meat. The mode of action is different between Flint and Moloney and the present invention. They are more concern on the quality of meat that any other factors. As explained supra the choice of antigen and the mode of administration are not the adequate.

Ohkaru et. al. and JP 02150294. If a monoclonal antibody is fed as is, meaning in a purified form, it may not survive the acidity of the stomach. The present invention suggest feeding the antibody in several forms, i.e. whole egg, spray dried whole egg, spray dried yolk, purified and encapsulated, this is not suggested in OhKaru or JP02150294. Weidemann, et. al. 1989 and 1990, showed that the antibody are more resistance to the acidity of the stomach if fed as a whole egg or protein extraction.

Combination Moloney (Livestock Prod, Sci. 1995, 42:239-245) and Flint (Proc. Nutrition Soc. 1992, 51:433-439) Ohkaru et al and JP 02150294. The examiner cites the following "That two things are actually equivalent, in the sense that they will both perform the same function, is not enough to bring into play the rule that when one of them is in the prior art the use of the other is obvious and cannot give rise to a patentable invention". If different compounds have the same function or result they are equivalent, inventor refers to patent against lipase inhibition, cck patents showed above where same results can obtained with drugs, antibodies and feed. They all are compounds that have the same results and they are seen as inventions. The present invention is not different from them even if anti-lipase antibody inhibit lipase it does it by a different way due to different source of the compound, different structurally compound, different mode of action and naturally produced.

Examiner suggests since a motivation to inhibit lipase existed, antibodies are know to inhibit lipase and antibodies are conventionally used in animal feed the invention is obvious. Inventor refers to patents William , et. al. US Patent #6,080,400, Kink , et. al. US Patent #5,736,139, Stolle, et. al. US Patent #5,932,250 and Kodama , et. al. US Patent

#6,419,9268 in which antibiotics have the same effect than avian antibodies. On patents by Stafford, et. al. US Patent #6,346,247 and Kink , et al. US Patent #6,395,273 immune suppressant drugs have the same effect than avian antibodies and Sterling, et. al. US Patent #5,753,228 the use of antihelmintic have the same effect than avian antibodies.

The problem with in-vivo and in-vitro depends on the form the product is delivered to the animal or human. If the antibody is fed as whole egg or yolk there is no need for enteric protection. If the antibody is purified then it is preferred to encapsulate the antibody. As explained supra the antibody resist gastric acidity when fed as whole egg or protein extraction. The difference in in-vivo and in-vitro response is basically that there are not interference of acidity or protease activity in an in-vitro system. It have been demonstrated that the antibody can reach the duodenum intact and can also be degraded as suggested by Coleman (US patent# 5,585,098), where it was found that the active part of the antibody or at least some active peptides can reach the mammary gland.

Claim Rejections Under 35 USC §112

Claims 8, 14, 18, 31, and 38 are rejected under 35 USC 112. The specification suggest the use of a porcine pancreatic extract containing lipase (page 4 of the specification). This pancreatic extract also contains other enzymes like amylase and proteases. In the specification by immunizing hens with this pancreatic extract hens produced antibodies not only to lipase but also to amylase and proteases, meaning that not only fat absorption is inhibited but also protein and carbohydrates. The specification only tested for the ability of the antibody extract to inhibit fat absorption but implied the inhibitions of other enzymes as on claim 24 now withdrawn. The inventor based on the different antibodies produced due to the immunization against porcine pancreas extract and since it does not add new material but emphasize what the specification suggested as originally filed, is suggesting the following as Claim 1:

Claim 1 (clean version)

A method for inhibiting nutrient digestibility in a mammal related to control animals by orally feeding said mammal an avian antibody against porcine pancreatic extract that binds lipase in the gastro-intestinal tract of said mammal.

Claim 1 (with corrections)

A method for inhibiting nutrient digestibility [pancreatic lipase so as to reduce fat absorption] in a mammal related to control animals by orally feeding said mammal an avian antibody against porcine pancreatic extract that binds [pancreatic] lipase in the gastro-intestinal tract of said mammal. [to inhibit the fat-hydrolyzing of said pancreatic lipase.]

New grounds of Objection, pg. 11 & 12 of paper No 31: the added material which is not supported by the original disclosure is as follows: "By inhibiting lipase through binding the ingested fat will not be absorbed and the fat itself will be excreted"; binding is between the antibody and lipase, examiner's objection is accepted.

Attached hereto is a marked-up version of the changes made to the claims.

Based on the above amendments and remarks, reconsideration an allowance of the pending application is believed to be warranted.

Respectfully submitted,

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Claim 1.

A method for inhibiting nutrient digestibility [pancreatic lipase so as to reduce fat absorption] in a mammal related to control animals by orally feeding said mammal an avian antibody against porcine pancreatic extract that binds [pancreatic] lipase in the gastro-intestinal tract of said mammal. [to inhibit the fat-hydrolyzing of said pancreatic lipase.]

Claim 8.

The method of claim 1wherein prior to the step of feeding said mammal said avian antibody, said antibody is produced in avian eggs.

Claim 14.

The method of claim 1 wherein prior to the step of feeding said avian antibody, said antibody present on whole egg, egg yolk or purified antibody, [the antibody] is first freeze dried or spray dried.

Claim 18.

The method of claim 1 wherein the orally fed antibody, said antibody present on whole egg, egg yolk or purified, is fed in a powder form

Claim 31.

The method of claim 1 wherein the orally fed antibody , said antibody present on whole egg, egg yolk or purified, is fed in a liquid form

Claim 38.

(Withdrawn) A method of altering absorption of fat of a mammal to inhibit the absorption of fat, comprising the steps of immunizing an animal with pancreatic lipase to produce pancreatic lipase antibody, and then orally administering said antibody to said mammal to

bind pancreatic lipase in its gastro-intestinal tract and thereby inhibit the fat hydrolyzing activity of said pancreatic lipase in said tract.

Claim 40

The method of claim 1 wherein the orally fed antibody, said antibody present on whole egg, egg yolk or purified, is fed in a enteric protected form.